

WHAT IS CLAIMED IS:

1. Modified TNF, comprising TNF covalently bound to between about five and twelve PEG molecules having an approximate weight average molecular weight in the range of about 10,000 to about 40,000.
- 5 2. The modified TNF of Claim 1 wherein said PEG is covalently bound to primary amine groups on said TNF through a biocompatible linker and where said PEG has an approximate weight average molecular weight in the range of about 20,000 to about 30,000.
3. The modified TNF of Claim 1 wherein said linker is selected from the group consisting of succinimidyl succinate, succinimidyl propionate, and N-hydroxy succinimidyl.
4. The modified TNF of Claim 2 wherein said linker is selected from the group consisting of succinimidyl succinate, succinimidyl propionate, and N-hydroxy succinimidyl.
- 15 5. The modified TNF of Claim 1 wherein said TNF is TNF- α .
6. The modified TNF of Claim 1 wherein said TNF is isolated human TNF.
7. The modified TNF of Claim 1 wherein said TNF is recombinant human TNF.
- 20 8. The modified TNF of Claim 1 wherein said TNF is human TNF mutated by deleting amino acids 1-9 of the mature TNF protein.
9. The modified TNF of Claim 1 wherein said TNF is human TNF mutated by changing the lysine at position 166 of the mature protein to alanine.
10. The modified TNF of Claim 1 wherein said TNF is human TNF mutated by changing the lysine at positions 188 and 204 of the mature protein to alanine.
- 25 11. Mutated TNF, comprising human TNF in which lysine at one or more of positions 166, 188 and 204 is changed alanine.
12. The mutated TNF of Claim 11 in which lysine at position 166 is changed to alanine.

13. The mutated TNF of Claim 11 in which lysine at both of positions 188 and 204 is changed to alanine.

14. A method of enhancing the circulating half life of TNF while reducing its toxicity comprising modifying said TNF by covalently bonding to it between about five and twelve PEG molecules having an approximate weight average molecular weight in the range of about 10,000 to about 40,000.

15. The method of Claim 14 in which said PEG is covalently bound to primary amine groups on said TNF through a biocompatible linker and where said PEG has an approximate weight average molecular weight in the range of about 20,000 to about 30,000.

16. A method of enhancing the tumoricidal activity of TNF comprising modifying said TNF by covalently bonding to it between about five and twelve PEG molecules each molecule having an approximate molecular weight of 20,000 to 30,000.

17. The method of Claim 16 in which said PEG is covalently bound to primary amine groups on said TNF through a biocompatible linker and where said PEG has an approximate weight average molecular weight in the range of about 20,000 to about 30,000.

18. A method of inhibiting tumor growth in a patient suffering from a tumor comprising administering to said patient a therapeutically effective amount of the modified TNF of Claim 1.

19. A method of inhibiting tumor growth in a patient suffering from a tumor comprising administering to said patient a therapeutically effective amount of the modified TNF of Claim 2.

20. The method of Claim 19 wherein said tumor is a melanoma.

21. The method of Claim 19 wherein said tumor is a colon cancer.

22. The method of Claim 19 wherein said tumor is a kidney cancer.

23. The method of Claim 19 wherein said tumor is a breast cancer.

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